

**Methods and Compositions for Expressing Heterologous Genes  
in Hepatocytes Using Hepadnaviral Vectors**

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**Abstract**

Methods and compositions for efficient, hepatocyte-specific delivery and expression of heterologous genes, both *in-vitro* and *in-vivo*, using hepadnaviral vectors are provided. Methods for expressing a heterologous gene in hepatocytes are provided  
10 involving: providing replication defective hepadnavirus particles at a titre level competent to infect hepatocytes, wherein a region of the preS/S-gene of the hepadnavirus genome has been replaced with the heterologous gene such that expression of the heterologous gene is regulated by regulatory sequences of the preS/S-gene; and  
15 infecting hepatocytes with the hepadnavirus such that the heterologous gene is delivered into the hepatocytes and expressed in the hepatocytes. Methods for treating a subject with a hepatic disorder (e.g., hepatitis infection) are also provided. Replication defective hepadnavirus particles, and pharmaceutical compositions thereof, are also provided. Methods of producing therapeutic replication defective hepadnavirus particles at a titre level suitable for therapeutic use are also provided.

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